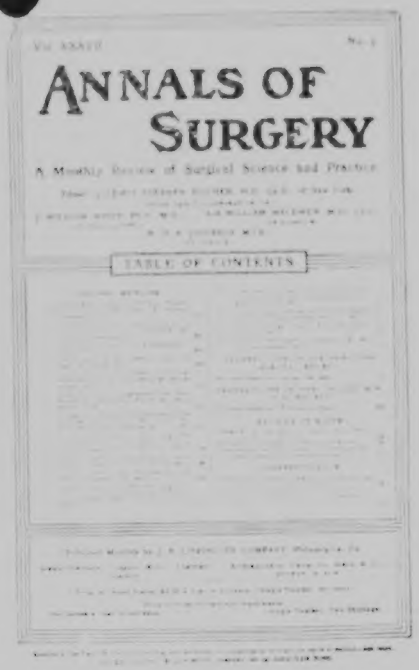

THE VALUE AND LIMITATION OF DIASTASE, UREA AND PHTHALEIN IN ESTIMATING RENAL FUNCTION IN ASSOCIATION WITH URETERAL CATHETERIZATION.

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REPRINTED FROM ANNALS OF SURGERY FOR DECEMBER, 1913
227 SOUTH SIXTH STREET, PHILADELPHIA, PENNA.

THE VALUE AND LIMITATION OF DIASTASE, UREA AND PHTHALEIN IN ESTIMATING RENAL FUNCTION IN ASSOCIATION WITH URETERAL CATHETERIZATION.

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RECENTLY Wohlgemuth [1] has introduced quantitative diastase estimation of the urine as a method of determining the relative functional capacity of the two kidneys. In a series of normal cases he found the diastatic activity the same, or practically the same, on each side, while in unilateral disease the diastase content of the urine from the pathological kidney was always lower than that from the normal kidney. Simultaneous determination of function by means of cryoscopy, phloridzin and indigo-carmine showed that a certain amount of parallelism existed between the findings of these various tests and the amount of diastase present. He suggests that the diastatic activity may be of value in determining the advisability of nephrectomy in certain instances.

In our previous communications [2] the undoubted value of phthalein in these connections was demonstrated. Urea, and in certain cases indigo-carmine, phloridzin and Albarran's polyuria test were utilized in conjunction with phthalein. Attention was called to a certain advantage which phthalein has over the other tests, viz., that it reveals not only the relative but the accurate absolute functional capacity of each kidney, thus allowing a prognosis concerning the ability of the remaining kidney to carry on unaided renal function. As

a result of these studies it was learned that the employment of all of the tests in any one case was impracticable, time consuming and also unnecessary, since the urea and phthalein furnish all available information. In a series of 40 cases the study of the phthalein output, of the urea per cent., total urea, and diastase from each kidney is here presented, an effort being made to determine the relative reliability and practicability of these tests as well as to ascertain what advantages, disadvantages and limitations pertain to each.

The Technic Employed.—The diastase has been determined according to the original technic of Wohlgemuth which is as follows: After neutralization, the same amount of urine from each side is placed by means of an accurately graduated pipette in a series of twelve test tubes in amounts decreasing from 0.6 c.c., 0.5–0.1–0.04 c.c. A sufficient quantity of 1 per cent. NaCl solution is then added to bring the amount of fluid in each tube up to 1 c.c.[1] To each tube is added 2 c.c. of a 1/1000 solution of freshly prepared soluble starch. The tubes are immersed in a water bath at 38° C. for 30 minutes after which they are placed in cold water for 3 minutes. To each tube is added sufficient 1/50 N. iodin solution to elicit a permanent color, violet or blue occurring where digestion is not complete. The tube in each series immediately preceding incomplete digestion of the starch indicates the diastase content of that particular urine and from this the *d* is calculated. *d* is the diastatic activity expressed as the number of c.c. of 1/10 per cent. starch solution capable of being digested by 1 c.c. of the urine utilized.

It might be emphasized that neutralization of the urine is important. In one case in which the urine on the left side was extremely alkaline, determined on the unneutralized sample, *d* was 4, whereas after neutralization it was 20. Although an extreme case this indicates the necessity of neutralization in every instance.

[1] One c.c. of urine was diluted to 10 c.c. and from this diluted urine the measurements of the amounts less than 0.1 c.c. were made.

Urea was determined in all of the earlier work by means of the Doremus method. In some of the later cases, however, Marshall's [8] new area method was utilized.

The phthalein test was utilized according to the technic described in previous communications, except that the drug was given always intravenously and collections made for 15 minutes or half-hour periods.

In forty cases fifty diastase determinations were made. The general result coincides fairly well with those of Wohlgemuth in that in the majority of instances the diseased or more diseased kidney is correctly indicated through the decreased diastatic activity of the urine from that kidney. Where the various tests harmonize no comment is necessary. One case, however, is of sufficient interest to justify a detailed report, because it afforded an opportunity for an extensive and prolonged study of function and also the opportunity to observe the effect of a pyelotomy on the function of the operated kidney, as well as the effect of this procedure and of the anæsthetic on the function of the other kidney.

There was complete blockage of the right ureter, the urine draining from a renal fistula, the result of an operation for a calculus seven years previously. The urine only from the left kidney passed through the bladder. This kidney contained in its pelvis a large calculus which was associated with a slight infection.

The total function was practically normal, 41 per cent. phthalein for one hour. All three tests indicated the left kidney to have a functional capacity double that of the right. At operation under gas and ether anæsthesia a large bifid kidney was encountered on the left side, the lower half showing a marked hydronephrosis, the upper half, healthy kidney tissue equal to the size of a normal kidney. The stone lay in the pelvis of the lower half and was removed through an incision in the pelvis (Dr. Young). Although no dissection was done to determine the exact anatomical condition present, it seemed very evident that the kidney had a double pelvis, the stone lying in the lower one, the upper pelvis entering into a common ureter below the stone and being consequently free of obstruction. This upper

hypertrophied kidney tissue explained the presence of the practically normal total function in the presence of these severe bilateral renal lesions.

The day after the operation (the right kidney not having been disturbed) the function of the right kidney dropped to one-half its previous capacity, while that of the left dropped to one-third, the function of two sides being now identical. The time of appearance from the right was 40 minutes as compared to 15 minutes prior to operation. The function of each kidney gradually improved until at the end of three weeks the level which existed previous to operation was reached.

In certain cases differences in functional capacity, as indicated by these various tests, exist, a consideration of the details of these differences furnishes information as to the relative value and limitations of each test.

In Case I there was a slight grade of pyelonephritis of the right kidney and some hydronephroses. The phthalein indicated the function of this kidney to be half that of the left, while the total urea indicated identically the same ratio. The diastase, however, showed a very much greater function on the left than on the right side, and when the greater quantity of urine from the left side is considered this disproportion would be even more exaggerated. The phthalein and total urea appeared to be more in accord with the clinical findings. In this instance the urea per cent. was of no value.

While from our results it is quite evident that differences in diastase are not so readily caused through dilution as differences in urea per cent., dilution in relation to diastase is not a negligible factor as is exemplified by one of our cases. In Case XI, a slight left-sided pyelitis, the phthalein was equal from the two sides, indicating equal function. This was corroborated by the total urea. The diastase showed a marked difference on the two sides. But if corrected for dilution the total diastatic activity would be practically equal.

In the presence of an unmistakable tuberculosis of the left kidney (Case XXXVI) in which the decreased function was indicated by phthalein, urea per cent. and total urea, the

diastase failed to reveal any differences in function. Total diastase, however, would be more in accord with the true functional condition, but this furnishes no information other than is available from phthalein and urea. Case XXVII is another instance of the same phenomenon.

In two other cases which clinically presented no signs or symptoms of renal disease, a marked difference in function on the two sides was indicated (Cases XIV and XX).

These six cases serve to demonstrate that diastase is not an infallible index of relative functional capacity, since in two apparently normal cases considerable differences existed between the two sides, in two cases a definite lesion was not indicated, in another the functional injury was exaggerated, while in the sixth case unless the quantity of urine was taken into consideration an erroneous impression of function was given.

The diastase is of very considerable value, however, in the majority of cases. It is about equal in value to urea per cent. In some cases it may be of even greater value than urea per cent. because of the fact that it is not so readily affected by dilution. In the cases of free urinary secretion, which are usually cases without ureteral inhibition, the phthalein gives much more accurate information and in such cases diastase and urea are of minor value only.

The employment of functional tests in association with ureteral catheterization is attended with two great difficulties which in certain cases make it impossible to obtain all desirable information from any one test: (1) Inhibition of function and (2) leakage around the ureteral catheter.

1. *Inhibition.*—Any discrepancy due to inhibition can be detected readily through the determination without ureteral catheterization of total renal function by phthalein and error can thereby be avoided. For instance, with a total phthalein excretion normal or nearly normal, one kidney at least is normal or practically so. If, in such a case, on ureteral catheterization one should find on one side decreased function, which under ordinary conditions would be an indication for

nephrectomy even though the function of the supposedly healthy kidney as estimated with the aid of the catheter showed an apparently dangerously low excretion on account of the inhibition, one need not hesitate about removing the diseased kidney. The low function here is clearly the result of inhibition, the extent of which is indicated by the discrepancy between the separated functions and the total function without ureteral catheterization.

In cases of bilateral tuberculosis, the amount of pus from each side being practically the same, the phthalein can demonstrate that one kidney has a function far in excess of the other—a function sufficiently good to allow of successful nephrectomy. However, in certain instances inhibition might be so marked and the elimination of phthalein from each side consequently so small that it might be impossible from phthalein alone to determine which is the better kidney. Here diastase and urea per cent. together with a difference in the intensity of urine pigment and a consideration of the total phthalein would be of value. No such instance, however, has yet been encountered. In the majority of cases the influence of inhibition can be minimized through longer collections (½ to 1 hour).

Occasionally owing to extreme nervousness on the part of the patient or on account of unusual pain attending the presence of the catheter in the ureter, the time of catheterization must be curtailed to such an extent that an accurate quantitative determination of function is impossible. Here one is obliged to secure all of the necessary information from microscopical and clinical data and from urea per cent., time of appearance of phthalein and possibly of diastase, provided sufficient urine has been excreted to allow the application of the tests.

2. *Leakage.*—In order to obtain an accurate quantitative estimation of the function of each side it is necessary to secure complete collection of the urine. By the use of Albarran's flute end catheter this is usually possible. In a certain proportion of cases, especially those with relaxed ureters, leak-

age does occur and sometimes in amounts sufficient to nullify the findings. Unless one repeats the catheterization, which is not always practicable, using the Garceau catheter on one side along with transvesical collection for the other, knowledge of the relative functional values must be largely obtained from urea per cent., diastase and time of appearance of phthalein. This was well illustrated in a case with normal kidneys in which so much leakage occurred that the estimation of the relative function from phthalein was impossible, but the diastase, urea per cent. and phthalein appearance time all indicated identical functional capacity on the two sides.

Combination of Tests.—The number of tests has increased to such an extent that the use of all of them is impracticable. It becomes necessary, therefore, to consider what tests are really necessary for all of the available information under all conditions. In order to make a judicious selection it is necessary that one be familiar with the peculiarities, advantages, disadvantages and limitations of each and all of the approved tests.

Interpretation of findings is not always easy but in order that this may be made simpler, our ideas relative to the indications for the employment of any one of these tests alone or in combination, together with the significance of their findings, are here presented.

The phthalein test is incomparable so far as total function is concerned and gives information frequently unavailable from any other source, and in cases in which leakage and inhibition are absent furnishes in itself all the information necessary in regard to the function of each kidney. The absolute on each side as well as the relative function is revealed.

It is advisable to give the phthalein intravenously and to make collections for one-half to one hour periods when an accurate quantitative knowledge of the function of each kidney is desired, because as was previously pointed out, short periods of collection are not reliable. In the majority of in-

stances, however, where it is necessary only to ascertain if the remaining kidney has a sufficiently good function to warrant operation, shorter periods (15 minutes) suffice.

In exceptional cases where marked inhibition or severe leakage occurs, diastase and urea per cent. may furnish most important information in conjunction with microscopical and clinical data. Diastase is subject to the same errors as urea per cent. except that it is not so readily influenced by dilution. The findings of either must be accepted with extreme caution and only when, for causes mentioned above, total urea and quantitative phthalein determinations are impossible.

The method of procedure which has furnished the greatest amount of information is as follows. In all cases demanding ureteral catheterization the total functional capacity is first determined by phthalein without ureteral catheterization. Where the total function is low a cryoscopy of the blood serum or a blood urea determination is made (Marshall's method). After ureteral catheters are in place and a flow of urine has become established the phthalein is given intravenously and the time of appearance on the two sides noted. Urine is then collected for periods of from 15 minutes to 1 hour starting from the first appearance of the drug, the length of the period depending upon the character of the information desired. Where leakage or inhibition of a grade sufficient to interfere with quantitative determinations does not occur, the quantity of phthalein from each side during a period of 15 minutes or preferably one-half hour is considered the index of the function of the individual kidney.

Total urea estimations almost invariably corroborate the findings of the phthalein as regards the relative function.

In the presence of considerable leakage dependence is placed upon the time of appearance of the phthalein, urea per cent. and diastase.

In the presence of inhibition the urea per cent. and diastase are the factors of greatest value taken in conjunction with the clinical findings.

Practicability of Tests.—The phthalein and Marshall's urea determinations are made with great ease and take but

little time. The diastase while exceedingly simple is time consuming. Freshly prepared soluble starch solution is needed anew each day and at least a half hour actual time is necessary for each test.

CONCLUSIONS.

1. That diastase is of value in the majority of cases in indicating which is the diseased or more diseased kidney.

2. That in the majority of instances it is not necessary and adds nothing to the information obtainable from the phthalein or urea determinations which are more easily made.

3. That in cases with leakage or serious catheter inhibition, but where sufficient urine to allow a diastase determination has been obtained, the test is of value.

4. That dilution affects the urinary diastase content to a less extent than it does urea per cent.

5. That dilution is not a negligible factor in regard to this test, total diastase content being at times of greater importance.

6. That neutralization of the urine is not a negligible factor in the technic of the test.

REFERENCES.

[1] Wohlgemuth: Zeitschr. f. ürologie, 1911, 5, p. 801.
[2] Rowntree and Geraghty: Jour. Phar. and Exp. Therapeutics, vol. i, 1910, p. 579; Archiv. Int. Med., 1912, 9, p. 284.
[3] Marshall: Jour. Biol. Chem., 1913, xv, p. 487.